Hepatitis C virus infection: Spread and impact in the Netherlands
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Citation for published version (APA):
This thesis presents multidisciplinary studies on the epidemiology and public health impact of hepatitis C virus (HCV) among the general Dutch population and presumed high risk groups, including HIV-infected individuals, migrants, people with multiple tattoos and piercings, and drug users. The thesis commences with an overview of the epidemiological, clinical, and molecular aspects of HCV (chapter 1).

HCV screening programs
HCV screening programs have been developed and implemented throughout the world, all within their own setting. Effective screening programs are urgently needed to provide undiagnosed hepatitis C virus (HCV)-infected individuals with therapy and limit the future burden of disease. In chapter 2 literature was systematically reviewed to examine characteristics and outcomes of HCV screening programs and focuses on strategies to identify HCV risk groups hidden among the general population. We conclude that up till now screening programs only identified a small proportion of the estimated population of HCV-infected individuals worldwide. The programs that were included in the review were very heterogenic in their organization, recruitment, and screening procedures and the vast majority did not use a comparison group to assess the effectiveness of their screening program. Furthermore, we found that a pre-screening selection based on risk factors can increase the efficiency of screening in low-prevalence populations. We recommend conducting programs with control groups to evaluate effectiveness. In addition, program characteristics such as type of diagnostic test, screening uptake, and clinical outcomes should be reported systematically.

HCV epidemiology among subpopulations in the general Dutch population
Men who have sex with men (MSM)
From 2000 onwards, HCV among HIV-infected MSM has emerged. In Chapter 3.1.1 we provide an expansive literature overview of sexually acquired viral hepatitis among MSM, using recent insights obtained through molecular epidemiology of HAV, HBV, and HCV. Chapter 3.1.2 describes the HCV prevalence and determinants among HIV-positive and HIV-negative MSM participating in a biannual survey of the STI outpatient clinic located at the Public Health Service of Amsterdam. Here we found a high and increasing HCV prevalence in HIV-infected MSM for the period 2007-2008. Rough sexual techniques and use of recreational drugs were associated with HCV-infection and phylogenetic analysis supported our hypothesis that HCV was sexual transmitted. In chapter 3.1.3, earlier results of chapter 3.1.2 were put in a larger timeframe and the HCV incidence was measured over a 15-year period (1995-2010) in the same setting. We found that HCV prevalence among HIV-positive MSM substantially increased over time from 5.6% in 1995 to 20.9% in 2008, but appears to have levelled off in recent years, possibly due to decreased risk behaviour as a consequence of increased awareness, saturation in the population, and earlier HCV screening and treatment. HCV prevalence among HIV-negative MSM remained low and stable (around 0.5%, 2007-2010).
Migrants
Little is known about the HCV prevalence in non-Western migrant populations. In chapter 3.2, to determine whether targeted HCV screening and prevention programs for migrants are needed, we examined the HCV prevalence and determinants among non-Western-migrants, Western migrants, and the native Dutch population in the Netherlands, with a special focus on the three largest migrant groups living in the Netherlands; people originating from Surinam, Morocco and Turkey. First-generation non-Western migrants are at increased risk for HCV except for migrants from Morocco and Turkey. Phylogenetic analysis suggests that transmission likely took place in the country of origin, causing introduction but no further transmission of endemic HCV strains in the Netherlands. We recommend that HCV screening and prevention programs should target first-generation, but not second-generation, non-Western migrants.

People with multiple tattoos and piercings
Chapter 3.3 describes the HCV and HBV prevalence among tattoo and piercing artists and people with multiple tattoos and piercings. According to the literature this group is at high risk for HBV and HCV. In this study we found no evidence for an increased HBV/HCV seroprevalence among persons with multiple tattoos and/or piercings living in the Netherlands. In total, 18/434 (4.2%, 95%CI: 2.64%–6.46%) participants were anti-HBc-positive and one was anti-HCV-positive (0.2%, 95%CI: 0.01%–1.29%). This finding might be due to the introduction of hygiene guidelines for tattoo and piercing shops in combination with the low observed prevalence of HBV and HCV in the general population. Tattoos and/or piercings, therefore, should not be considered risk factors for HBV and HCV among the Dutch population.

Treatment and future burden of HCV in injecting drug users (IDU)
In chapter 4.1 the results are shared of an HCV program offering HCV testing and treatment in a multi disciplinary setting targeted at IDU with chronic HCV (Drug Users Treatment Chronic Hepatitis-C, DUTCH-C). Results of this study show that in a multidisciplinary setting, HIV-negative drug users with chronic HCV infection can be treated successfully despite active drug or alcohol use and psychiatric diseases. In Chapter 4.2 we predict the future burden of disease in the IDU group and the role of HCV treatment and HIV co-infection. Due to a high competing mortality rate, particularly caused by HIV infection, and HCV treatment the burden of disease for HCV among IDU has been reduced. From 2011 to 2025, the HCV-related disease prevalence will rise by 36%, and would have been 33% higher in the absence of HIV. A further reduction can be achieved through improved treatment uptake and outcomes.

Cost-effectiveness of HCV screening
Since pregnant women are already routinely screened for several infectious diseases, we hypothesized that adding HCV screening to a routine screening could be cost-effective. In chapter 5 we found that implementing HCV screening during pregnancy in an already routine screening on infectious diseases is not cost-effective for pregnant women in general. However, adding HCV screening for first-generation non-Western women shows a modest cost-effective outcome and would argue in favour of the implementation of HCV screening. In addition, improved treatment outcomes with shorter treatment duration are expected in the coming years, further enhancing cost-effectiveness.
Discussion and conclusion
Finally, in chapter 6 we discuss the main findings of our studies. The epidemiology of HCV has changed over time. Screening should therefore be targeted at HIV-infected MSM, first-generation migrants, people who are at low risk (combined group of individuals who not consider themselves as a traditional risk group) and IDU. However, in the Netherlands data on the diagnosed population by risk group are scarce and research is needed to gain more insight into the undiagnosed in order to set up more efficient screening programmes. Recent screening programs aimed at the general population in the Netherlands have proven to be suboptimal partly because of the regional and temporal context. A universal screening program combining HCV and HBV, particularly targeting first generation non-Western migrants, should be considered, but more research is needed to gain insight into which specific migrant groups to target and the most effective approach for screening. Furthermore, we need to continue monitoring groups at possible risk for HCV such as HIV-negative MSM and young drug users.